REMARKS

Claims 1, 5-9, 21 and 22 are pending in this application.

I. Claim Rejections – 35 USC §103

1. Claims 1 and 7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245).

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143 - §2143.03 for decisions pertinent to each of these criteria.

The examiner failed to establish the *prima facie* case of obviousness because the above three basic criteria are not met.

First, the quantitation step is neither suggested nor taught by Palmirotta et al. or in combination with Hoglund et al.

Claims 1, 21 and 22 recite quantitating the human DNA by comparing the amplified DNA with a reference. The quantitation step is not found in Palmirotta et al. in view of Hoglund et al. The examiner argued that the quantitation step is found in Figure 1 of Palmirotta et al. The Figure 1 in Palmirotta et al. merely shows that the sample is originated from primate or nonprimate. The examiner confused the mere detection of the band or the relative comparison of the bands in Palmirotta et al. or in combination with Hoglund et al. with the quantitation step recited in claims 1, 21 and 22. Quantitation means the measurement of a quantity. Figure 1 itself includes only one human sample (Lane 1). From Figure 1, the quantity of human DNA (e.g., Lanes 14 and 15) cannot be measured.

The examiner further argued that claim 7 recites the quantitation step as comprising detecting the human DNA on an agarose gel stained with ethidium bromide, and it is not understood how Applicant can argue that the quantitation step is neither taught nor suggested by Palmirotta et al. or Carroll et al. Please note that claim 7 depends from claim 1," and that dependent claims must be read as if the language of the claim or claims from which it depends were also part of the dependent claim. Thus, claim 7 must be read as if "quantitating the human DNA by comparing the amplified DNA with a reference" in claim 1 from which claim 7 depends is also part of the dependent claim. Therefore, "comparing the amplified DNA with a reference for a quantitation assay" must be incorporated in claim 7. The recited references (e.g., Palmirotta et al. or in combination with Hoglund et al.) compare the amplified DNA with a reference which is related for the qualitative analysis or the comparison of the primate DNA band with the non-primate DNA band rather than the quantitation analysis of the human primate

DNA. Merely comparing the amplified DNA with a reference which is not related to the human primate DNA quantitation analysis cannot be equivalent to the quantitation step recited in claims 1 and 7.

There is no reason to make a reference for quantitation and compare the amplified DNA with the reference for the quantitation because the purpose of Palmirotta et al. is to determine the origin and gender of dried blood on a statue of the Virgin Mary. That is, there is no suggestion or teaching to perform the quantitation step in Palmirotta et al. or in combination with Hoglund et al. Also, there is no desirability of adding the quantitation step.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

Therefore, claims 1 and 7 are not obvious over Palmirotta et al. in view of Hoglund et al.

Second, the examiner failed to show that the feature of "said Alu element being enriched in the human genome compared to non-human primates genomes."

The examiner argued that this feature is shown in Figure 1, lanes 9-15 of Palmirotta et al. However, Lanes 9-15 of Figure 1 are not for non-human primates, but for mouse, ox, pig, etc. Palmirotta et al. expressly admitted that from Figure 1 it can be concluded that the statue blood originated from humans or from a non-human catarrhine primate. (See page 432, second column last three lines and page 433, first column, first two lines). That is, from figure 1, it cannot be determined whether the statue blood originated from humans or from a non-human catarrhine primate. Hoglund et al. does not teach this feature, either. In Hoglund et al., the Alu PCR is used

to distinguish the human material from the hamster material. The primers used in Hoglund et al. are ALI3 and ALI5, which are generic to the primates rather than specific to the human primates.

Since the feature of "said Alu element being enriched in the human genome compared to non-human primate genomes" is not found in the references, claims 1, 7, 21 and 22 and their dependent claims are patentable.

Third, there is no suggestion or motivation to combine reference teachings.

The purpose of Palmirotta et al. is to determine the origin and gender of dried blood on a statue of the Virgin Mary, whereas the purpose of the intra-Alu PCR in Hoglund et al. is to distinguish the human material from the hamster material. Furthermore, Hoglund et al. uses Alu PCR to distinguish the human material from the hamster material rather than non-human primates. The primers used in Hoglund et al. are ALI3 and ALI5, which are generic to the primates rather than specific to the human primates. There is no motivation to use intra-Alu PCR of Hoglund et al. in Palmirotta et al. Additionally, as admitted by the Examiner, Hoglund et al. further characterized the sample DNA by using inter-Alu PCR. That is, there is no motivation to replace the PCR of Palmirotta et al. with the PCR of the Hoglund et al.

The examiner argued that "the motivation to do so, provided by Hoglund et al., would have been to identify human DNA by amplifying ALU repeats." As stated above, like the primers in Palmirotta et al., the primers in Hoglund et al. are not specific to the human primates, but are generic to the primates. The examiner improperly inferred that ALI3 and ALI5 are specific to the human primate DNA merely on the basis of that ALI3 and ALI 5 may be used for identifying the hybrids retaining human material in the process of generating somatic cell hybrids using a human-hamster cell hybrid. The PCR using the primers ALI3 and ALI5 used in

Hoglund et al. may distinguish hybrids retaining human material from hamster material, but the PCR using the primers ALI3 and ALI5 cannot distinguish the human primate DNA from the non-human primate DNA. There is no advantage of using the primers and PCR of Hoglund et al. instead of the PCR in Palmirotta et al.

The examiner repeatedly rejected claims based on the possibility of the combination.

The examiner should provide why the use of the PCR of Hoglund et al. is more desirable compared with the PCR of Palmirotta et al. There is no motivation to combine the references.

The examiner's reasoning is at most that the references can be combined or modified, or that modifications of the prior art to meet the claimed invention would have been within the ordinary skill of the art.

It should be noted that (1) the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990); and (2) a statement that modifications of the prior art to meet the claimed invention would have been "'well within the ordinary skill of the art at the time the claimed invention was made'" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). See also *In re Kotzab,* 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000).

Since the examiner failed to establish a *prima facie* case of obviousness, withdrawal of the rejection is respectfully requested.

Therefore, claims 1, 21 and 22 are patentable, and their dependent claims 5-9 are also patentable.

2. Claims 1, 7, 21 and 22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245).

First, the quantitation step is neither suggested nor taught by Carroll et al, or in combination with Hoglund et al.

Claims 1, 7, 21 and 22 recite quantitating the human DNA by comparing the amplified DNA with a reference. The quantitation step is not found in Carroll et al. in view of Hoglund et al. The examiner argued that the quantitation step is found in page 38, col. 2, paragraph 1 of Carroll et al. However, Carroll et al. merely discloses that PCR products can be directly visualized using UV fluorescence. This is not a quantitation step, but a qualitative assay step. The purpose of Carroll et al. is to analyze human genome diversity. There is no suggestion or teaching to perform the quantitation step in Carroll et al. The examiner confused the possibility of quantitation with the actual quantitation step.

As stated above, claim 7 must be read as if "quantitating the human DNA by comparing the amplified DNA with a reference" in claim 1 from which claim 7 depends is also part of the dependent claim. Therefore, "comparing the amplified DNA with a reference for a quantitation assay" must be incorporated in claim 7. The recited references (e.g., Carroll et al. or in

combination with Hoglund et al.) compare the amplified DNA with a reference which is related for the qualitative analysis or the comparison of the primate DNA band with the non-primate DNA band rather than the quantitation analysis of the human primate DNA. Merely comparing the amplified DNA with a reference which is not related to the human primate DNA quantitation analysis cannot be equivalent to the quantitation step recited in claims 1, 7, 21 and 22.

Therefore, withdrawal of the rejections of claims 1, 7, 21 and 22 and their dependent claims is respectfully requested.

Second, there is no suggestion or motivation to combine reference teachings.

The purpose of Carroll et al. is to determine the human genomic diversity, whereas the purpose of the intra-Alu PCR in Hoglund et al. is to distinguish the human material from the hamster material. The examiner improperly guessed that ALI3 and ALI5 are specific to the human primate DNA merely on the basis of that ALI3 and ALI 5 may be used for identifying the hybrids retaining human material in the process of generating somatic cell hybrids using a human-hamster cell hybrid. The primers used in Hoglund et al. are ALI3 and ALI5, which are generic to the primates rather than specific to the human primates. There is no motivation to use intra-Alu PCR of Hoglund et al. in Carroll et al. In addition, as admitted by the Examiner, Hoglund et al. further characterized the sample DNA by using inter-Alu PCR. That is, there is no motivation to replace the PCR of Carroll et al. with the PCR of the Hoglund et al. which is not specific to the human primate DNA.

The examiner improperly rejected claims based on the possibility of the combination.

Therefore, withdrawal of the rejections of claims 1, 7, 21 and 22 and their dependent claims is respectfully requested.

Third, Carroll et al. in view of Hoglund et al., does not teach or suggest the present invention.

Please note that the corresponding author of Carroll et al. is Dr. Batzer, who is one of the inventors of the present invention.

The fact that the specific sequences are found as a 100% match within a theoretical consensus (or average) sequence of primate mobile elements (Alu) in general (about 300 bp) in no way suggests the knowledge or intention of having any clue about actually isolating these particular short sequences for 1) use as PCR primers; 2) Intra-Alu PCR amplification from young human specific elements (in contrast to the theoretical concept of Alu elements in general common to all primate species or limited subsets of species); 3) for quantitation (not just detection) of human DNA.

For the foregoing reasons, withdrawal of the rejections of claims 1, 7, 21 and 22 and its dependent claims is respectfully requested.

3. Claim 5 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252).

Claim 5 depends from claim 1. The applicant explained why claim 1 is patentable. Accordingly, claim 5 is also patentable.

In addition to the arguments above for claim 1, the examiner failed to establish a *prima facie* case of obviousness for the following additional reasons.

The examiner merely argued that the motivation is 100% local similarity of the instant primers in the sequence provided by Jurka. It is not well understood why 100% local similarity suggests the desirability of the combination or the desirability of the claimed sequences. Unlike the examiner's reasoning, Jurka merely discloses the comparison of Alu Sb1 subfamily consensus sequence with Alu Sb2 family consensus sequence, but does not disclose the specific primers. It is hardly understood how the ordinary skilled person can use the claimed sequences in view of Jurka and/or in combination with the other references. The examiner's reasoning is that, if the human genome sequences are known, all the primers based on that sequence are also obvious. This reasoning cannot be acceptable. There is no desirability of using the claimed sequences on the basis of the prior art references.

As stated above, the fact that the specific sequences are found as a 100% match within a theoretical consensus (or average) sequence of primate mobile elements (Alu) in general (about 300 bp) or small groupings or subfamilies of the elements in no way suggests the knowledge or intention of having any clue about actually isolating these particular short sequences for 1) use to design PCR primers; 2) Intra-Alu PCR amplification from young human specific elements (in contrast to the theoretical concept of Alu elements in general common to all or some primate species); 3) for quantitation (not just detection) of human DNA.

Since the examiner failed to establish a *prima facie* case of obviousness, withdrawal of the rejection is respectfully requested.

4. Claims 6 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245), in further view of Batzer et al. ("Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, Pages 3-6).

Claim 6 depends from claim 1. The applicant explained why claim 1 is patentable. Accordingly, claim 6 is also patentable.

In addition, as stated above, the fact that the specific sequences are found as a 100% match within a theoretical consensus (or average) sequence of primate mobile elements (Alu) in general (about 300 bp) in no way suggests the knowledge or intention of having any clue about actually isolating these particular short sequences for 1) use as PCR primers; 2) Intra-Alu PCR amplification from young human specific elements (in contrast to the theoretical concept of Alu elements in general common to all or subsets of primate species); 3) for quantitation (not just detection) of human DNA. Furthermore, the specific sequences of claim 6 (SEQ ID NO: 5 and SEQ ID NO: 6) were designed across a 12 bp deletion and other specific nucleotide mutations diagnostic to the AluYd6 subfamily of human specific Alu elements. These sequences are NOT found as a 100% match in Carroll et al., Hoglund et al., or Batzer et al. Knowledge of the Yd6 subfamily consensus sequence was not available until 2003 (Xing, et al. "Comprehensive Analysis of Two Alu Yd Subfamilies" Journal of Molecular Evolution. 2003. 57:s76-s89). Therefore, the sequences of claim 6 are completely unique to the present invention.

Therefore, claim 6 is patentable.

5. Claims 8 and 9 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245), in view of Gelmini et al. ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

Claims 8 and 9 depend from claim 1. The applicant explained why claim 1 is patentable. Accordingly, claims 8 and 9 are also patentable.

In addition to the arguments above for claim 1, the examiner failed to establish a *prima facie* case of obviousness for the following additional reasons.

Additionally, there is no suggestion or motivation to combine reference teachings.

The purpose of Palmirotta et al. is to determine the origin and gender of dried blood on a statue of the Virgin Mary, the purpose of the intra-Alu PCR in Hoglund et al. is to distinguish the human material from the hamster material, and the purpose of Carroll et al. is to determine the human genomic diversity based upon locus specific insertion presence or absence. Since the purposes of the above references are not related to the quantitation step, there is no reason to perform a quantitation step in view of Gelmini et al.

The examiner merely argued the advantages of using fluorogenic probes in quantitative polymerase chain reaction-based homogeneous assay is a motivation to combine the references,

but did not provide why the quantitation assay should be used or desirable in Palmirotta et al., Carroll et al., and/or Hoglund et al.

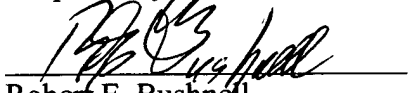
Since the examiner failed to establish a *prima facie* case of obviousness,

Therefore, claims 7, 8 and 9 are patentable.

No fees are incurred by this Amendment.

In view of the above, all claims are submitted to be allowable and this application is believed to be in condition to be passed to issue. Reconsideration of the rejections is requested. Should any questions remain unresolved, the Examiner is requested to telephone Applicant's attorney.

Respectfully submitted,



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